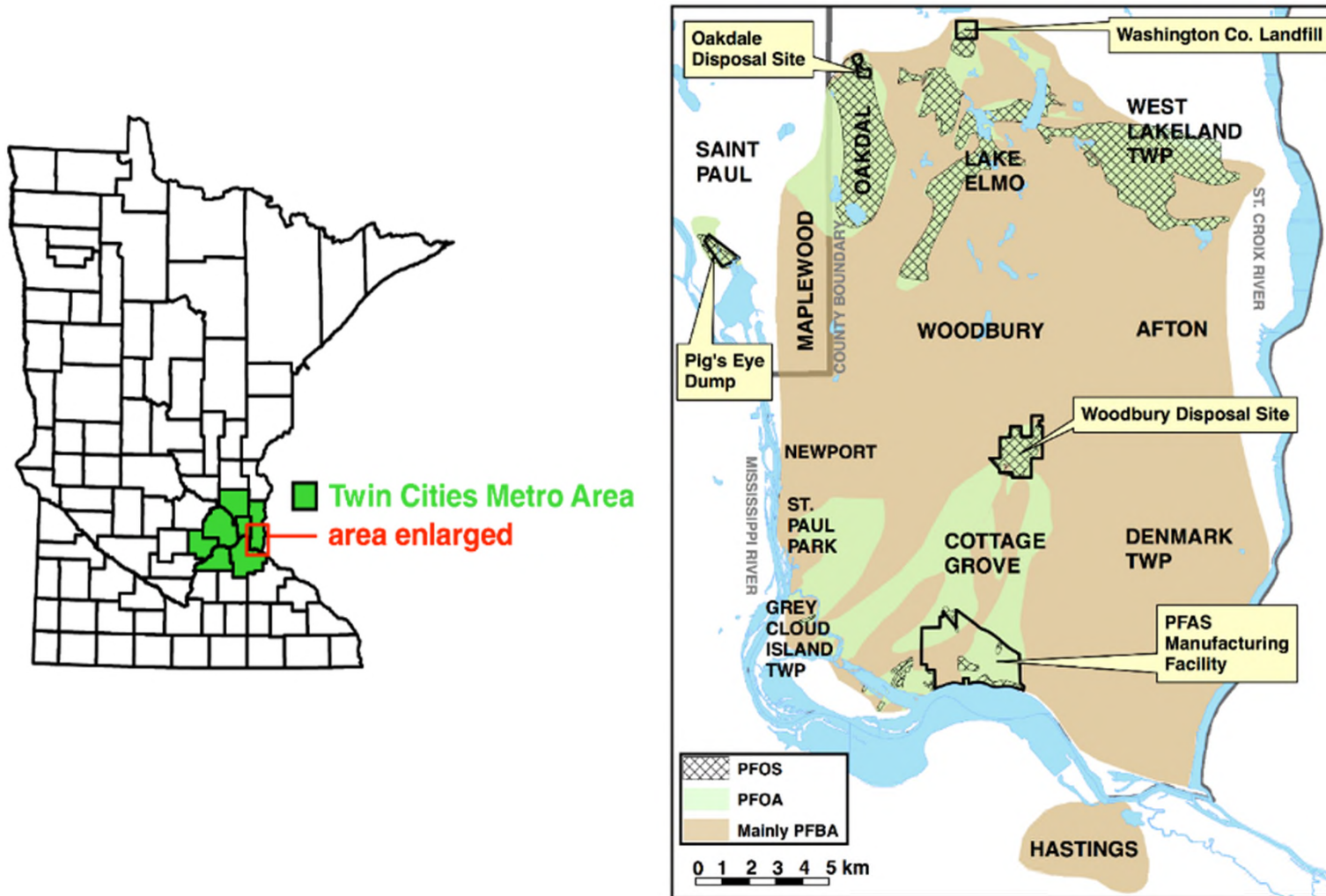


A Public Health Response to Large-Scale PFAS Contamination in Minnesota

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Denver, Colorado

PFAS in the Twin Cities



- PFAS a known issue in East Metro since 2002
- Contamination zone >150 sq. mi.
- 140,000 residents affected
- 2,700 private drinking water wells sampled
- Over 1,100 drinking water advisories issued
- Biomonitoring of residents

Drinking Water Guidance in Minnesota

MDH has programs to develop Health-Based Guidance (HBG) for conventional and emerging drinking water contaminants

2002: derived water guidance for PFOS and PFOA

2007 – 2009: revised PFOS and PFOA values and derived new values for PFBA and PFBS. For PFHxS, PFOS HBG was recommended as a surrogate

$$\text{nHBG} \left(\frac{\mu\text{g}}{\text{L}} \right) = \frac{\text{RfD} \left(\frac{\text{mg}}{\text{kg} \cdot \text{day}} \right) \times \text{RSC} \times 1000 \frac{\mu\text{g}}{\text{mg}}}{\text{IR} \left(\frac{\text{L}}{\text{kg} \cdot \text{day}} \right)}$$

Drinking Water Guidance in Minnesota

RfD = toxicological reference dose; may be developed for multiple exposure durations

IR = water intake rate; time-weighted, consumer-only intakes may be applied for short durations or over a lifetime

RSC = Relative Source Contribution factor to allocate the RfD across multiple exposure sources, including non-drinking water sources

$$\text{nHBG} \left(\frac{\mu\text{g}}{\text{L}} \right) = \frac{\text{RfD} \left(\frac{\text{mg}}{\text{kg} \cdot \text{day}} \right) \times \text{RSC} \times 1000 \frac{\mu\text{g}}{\text{mg}}}{\text{IR} \left(\frac{\text{L}}{\text{kg} \cdot \text{day}} \right)}$$

Past PFAS guidance used the standard equation shown, but we had outstanding concerns regarding early life exposures for the bioaccumulative PFAS

The Challenge of PFAS

Some PFAS are bioaccumulative

Serum concentrations do not represent recent exposure, but rather an integral of past exposure, attenuated over time

Serum concentrations are better than current intake as a measure of potential for health effects

Placental and breast milk transfer further complicate evaluation through “traditional” methods

PFAS	RfD (mg/kg-d)	Equivalent serum conc. (µg/L)*
PFOA	0.000018	130
PFOS	To be released ~4/3/19	
PFHxS	To be released ~4/3/19	

* Serum concentration is based on population-based parameters and should not be used for interpreting serum levels in individuals or for clinical assessment.

Concept for PFAS Exposure Model

a single-chemical,
one-compartment,
Excel-based,
lifetime-duration,
toxicokinetic (TK) model
to simulate serum levels of PFAS
from birth through adulthood
(attainment of steady-state
conditions)

- Start at birth with body burden from placental transfer
- Daily intake and elimination
 - Breastfeeding
 - Water Consumption
- 20,000-day simulation period

Governing Equations

Volume of Distribution (V_d) is chemical-specific and varies with age

Half-life is chemical-specific

$$\text{Serum Concentration} \left(\frac{\text{mg}}{\text{L}} \right) = \frac{\text{Dose} \left(\frac{\text{mg}}{\text{kg} \cdot \text{day}} \right)}{\text{Clearance Rate} \left(\frac{\text{L}}{\text{kg} \cdot \text{day}} \right)}$$

where:

$$\text{Clearance Rate} \left(\frac{\text{L}}{\text{kg} \cdot \text{day}} \right) = V_d \times k$$

$$V_d = \text{Volume of Distribution} \left(\frac{\text{L}}{\text{kg}} \right)$$

$$k = \frac{\ln(2)}{\text{half-life (days)}}$$

Initial Conditions

At Day 1 (birth):

$$\text{Serum Conc.} \left(\frac{\text{mg}}{\text{L}} \right) = \text{Maternal serum conc.} \left(\frac{\text{mg}}{\text{L}} \right) \times \text{placental transfer factor}$$

For all subsequent days:

$$\text{Serum Conc.} \left(\frac{\text{mg}}{\text{L}} \right) = \left[\text{Prev. day Serum Conc.} \left(\frac{\text{mg}}{\text{L}} \right) + \frac{\text{Today's Intake}(\text{mg})}{V_d \left(\frac{\text{L}}{\text{kg}} \right) \times \text{BW}(\text{kg})} \right] \times e^{-k}$$

Daily intake derived from contaminated water of known concentration, and/or breast milk with PFAS concentration calculated from transfer factor

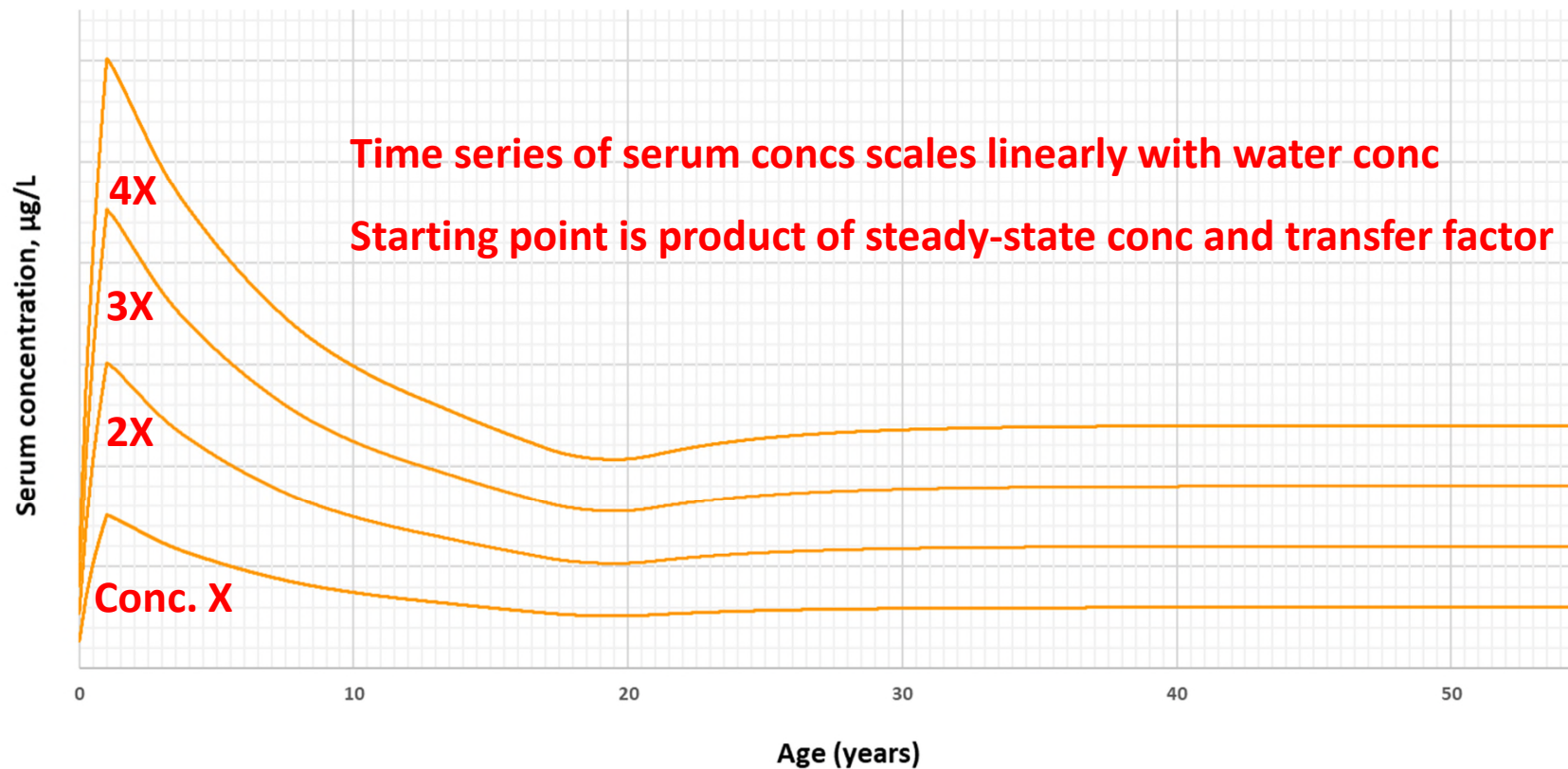
Maternal loss of PFAS during breastfeeding also considered

Key Parameters

Model Parameter	PFOA	PFOS	PFHxS
Half-life	840 days	1241 days	1935 days
Volume of Distribution (V_d)	0.17 L/kg	0.23 L/kg	0.25 L/kg
V_d Age Adjustment	2.4 at birth, 2.1 age 1-30 days, declines to 1 at age 10 years		
Clearance rate (CR)	0.00014 L/kg-d	0.00012 L/kg-d	0.000090 L/kg-d
Placental transfer factor (% of maternal serum level)	87% [range ~70 – 124%]	40% [range ~30 – 60%]	70% [range 43-95%]
Breastmilk transfer factor (% of maternal serum level)	5.2% [range ~3 – 11%]	1.7% [range ~1 – 2%]	1.4% [range 0.8 – 2%]

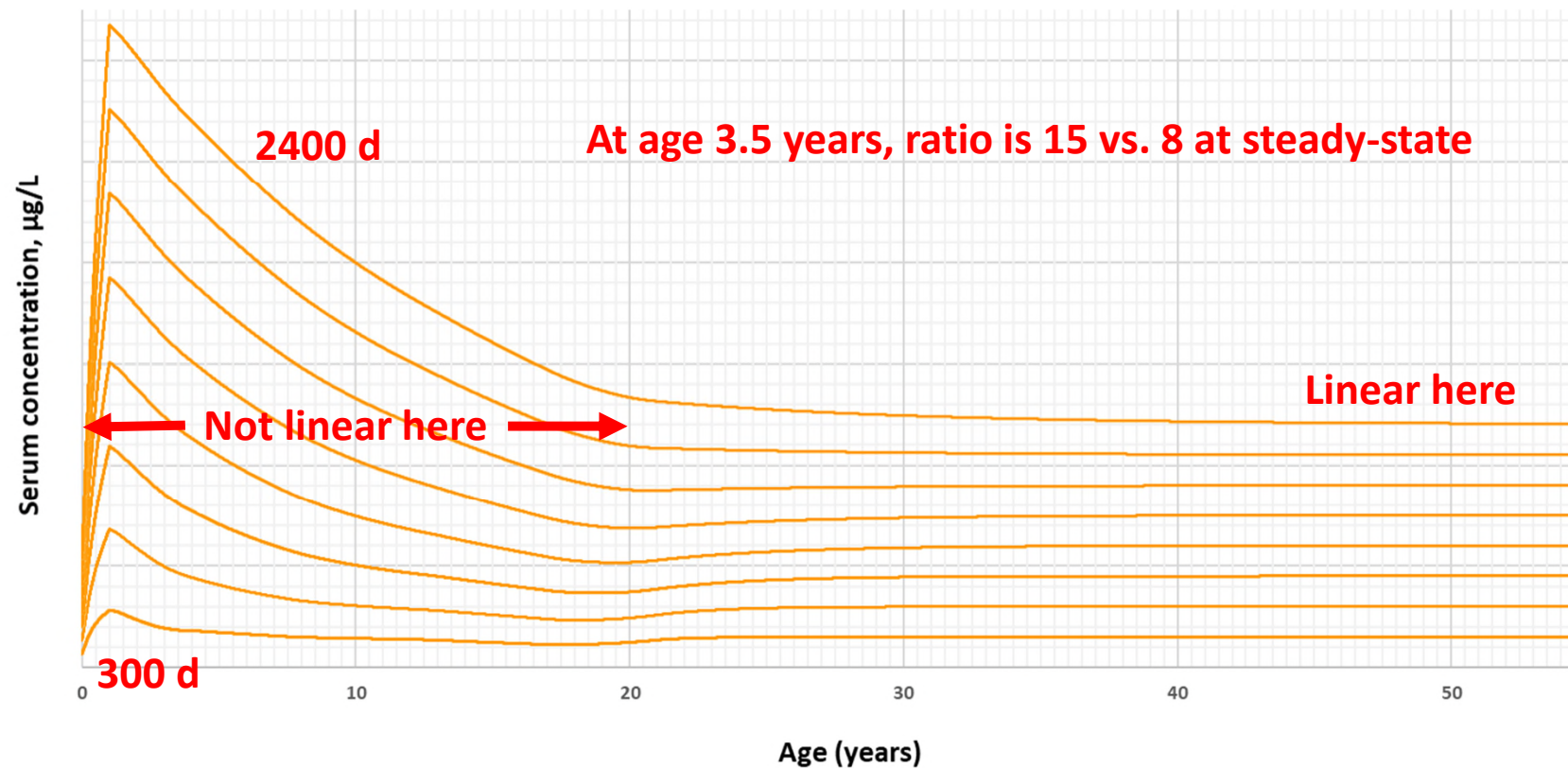
Using the Model

Generic Example– Effect of altering PFAS concentration in water

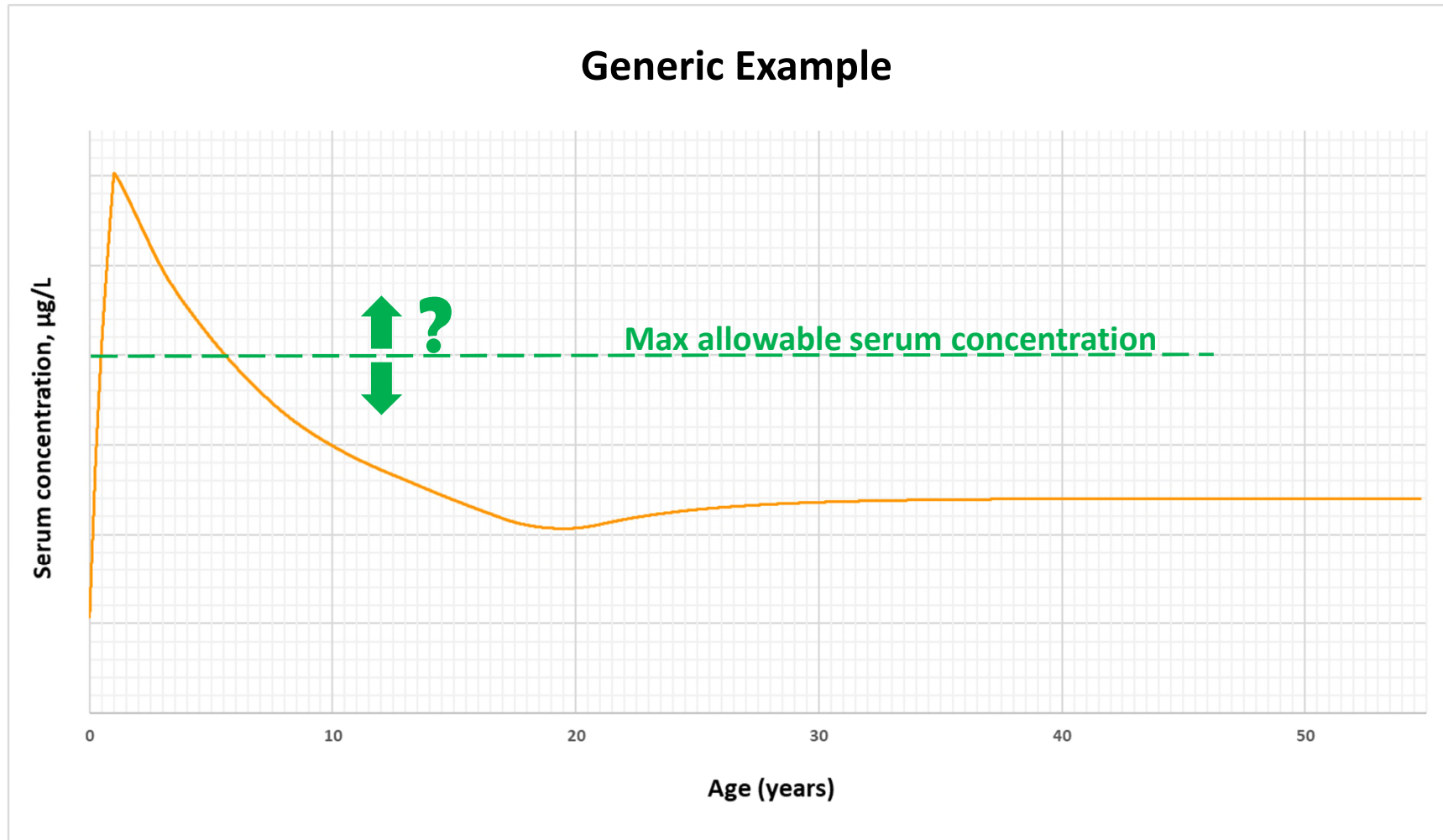


Using the Model

Generic Example– Effect of altering elimination half-life



Using the Model



Using the Model: RSC

Relative Source Contribution (RSC) factors

Derived by comparing RfD-based serum concentration to known *non-water-related* serum PFAS levels in the general population (NHANES and Minnesota-specific studies)

When non-water exposures are significant, RSC can be based on (or informed by) a residual value

Example (PFOA):

Reference serum conc. = 130 µg/L; 80% of this = 104 µg/L

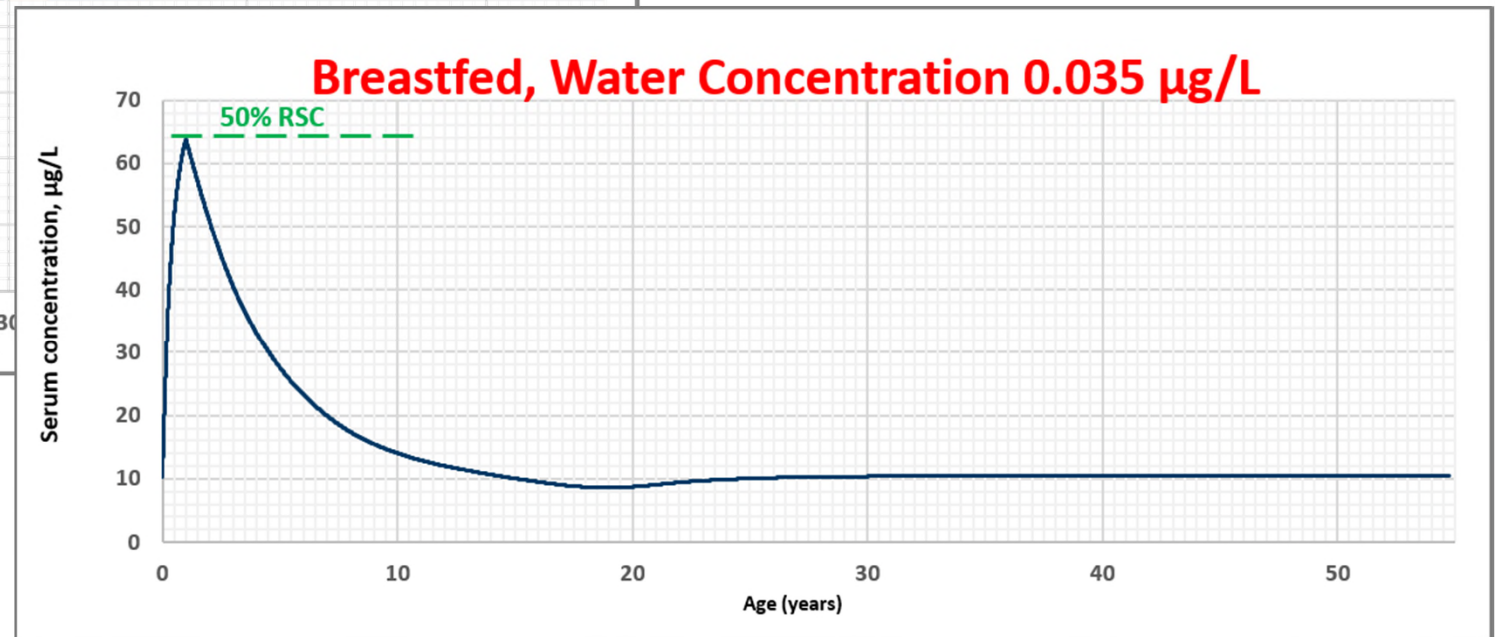
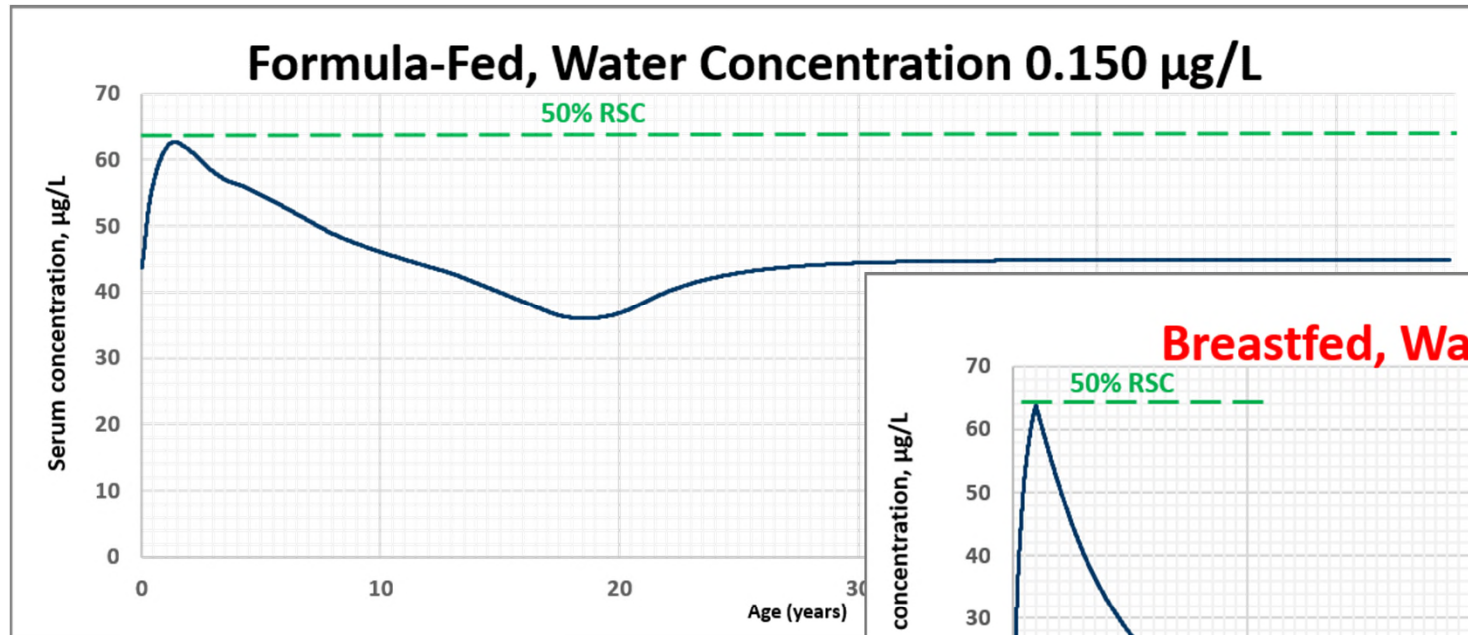
NHANES 2013-14 indicates P95 serum concentration of 5.57 µg/L

$104 - 5.57 = 98.4$ µg/L, which is about 75% of the reference serum concentration

This value was lowered to 50% due to uncertainties in the serum data, especially among younger children and infants, and following EPA's Exposure Decision Tree process for RSC (EPA, 2000)

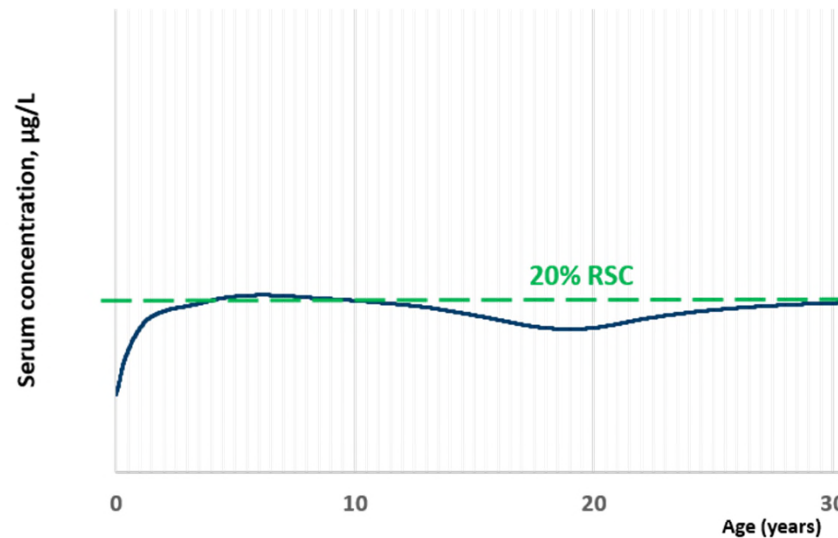
When non-water exposures are not significant, decision tree process leads to an RSC of 50% (example: PFHxS)

Model Output: PFOA



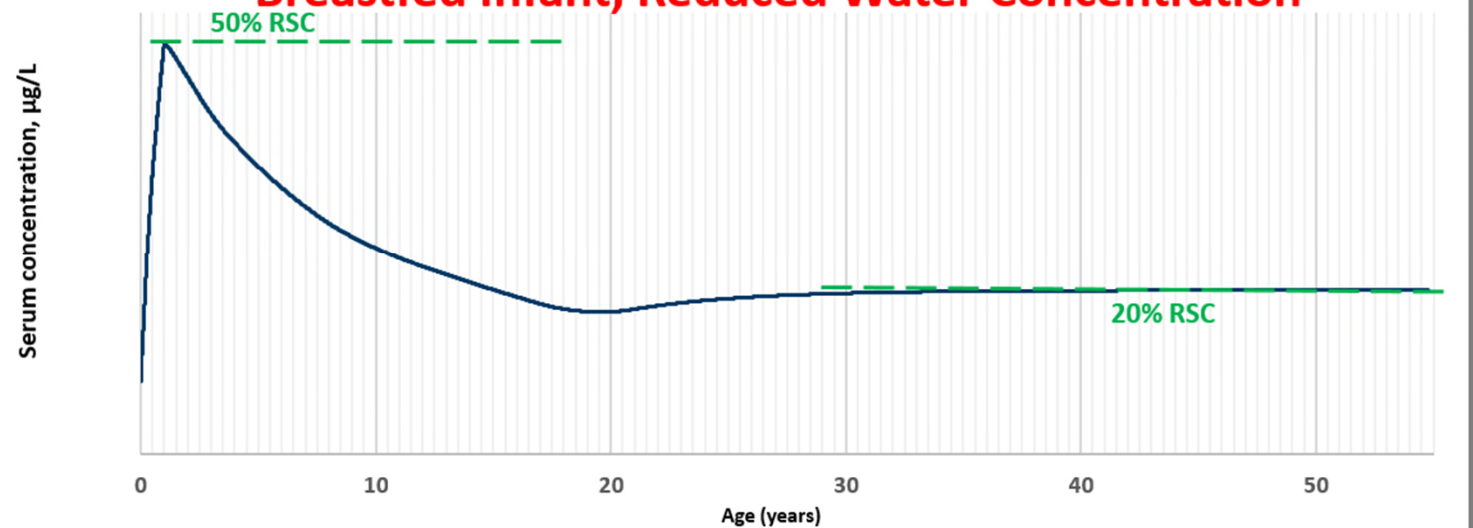
Model Output: PFOS

Formula-Fed Infant

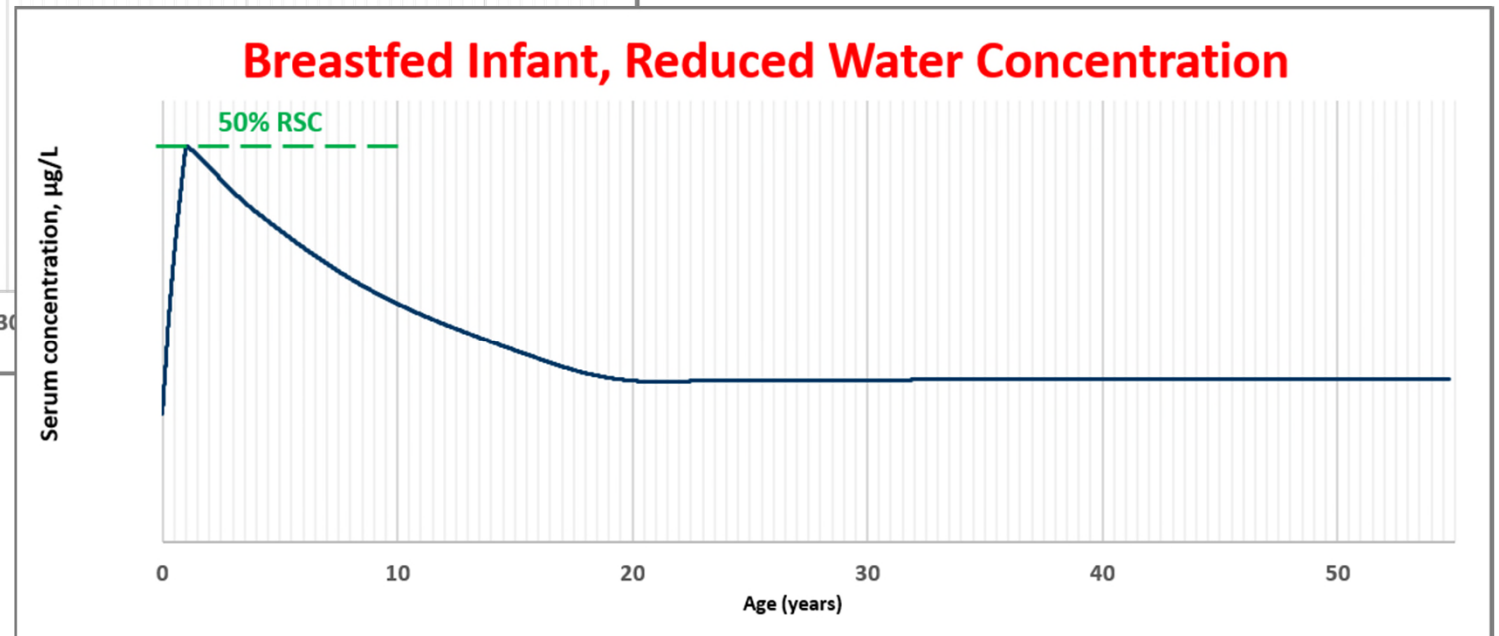
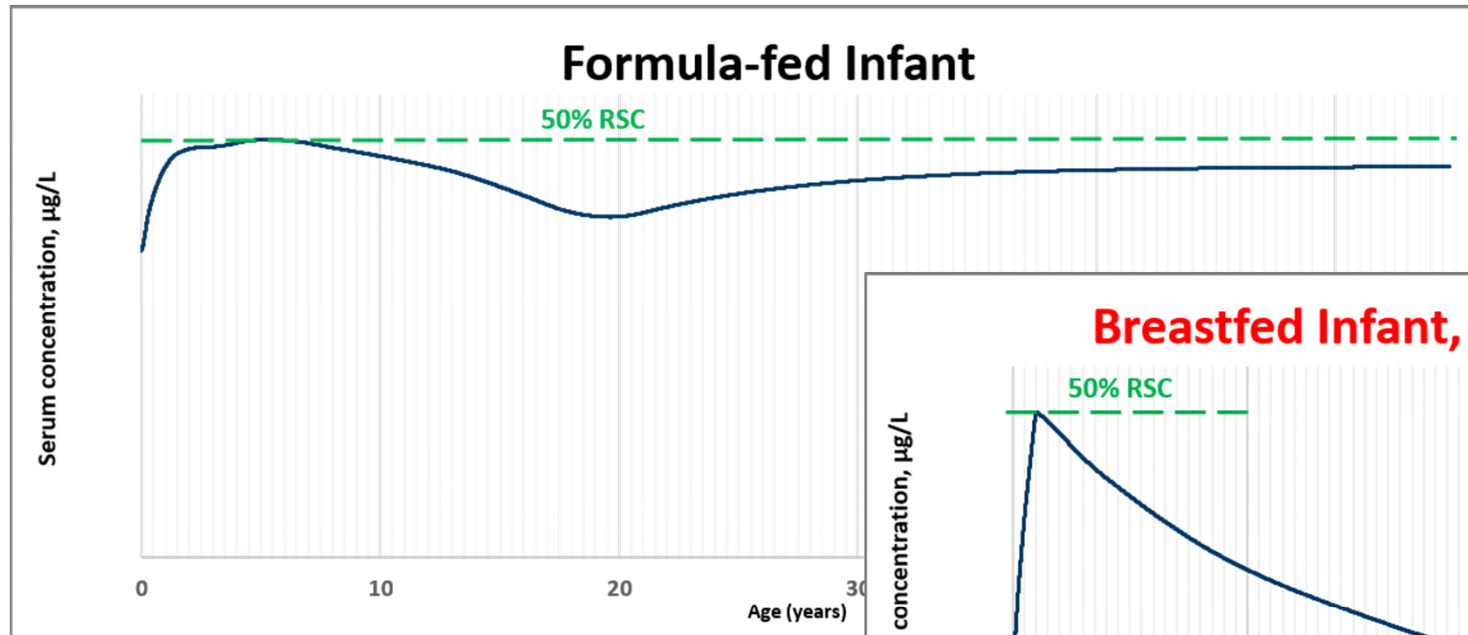


RSC = 50% (infants/young children)
RSC = 20% (older)

Breastfed Infant, Reduced Water Concentration



Model Output: PFHxS



Breastfeeding vs. Formula feeding

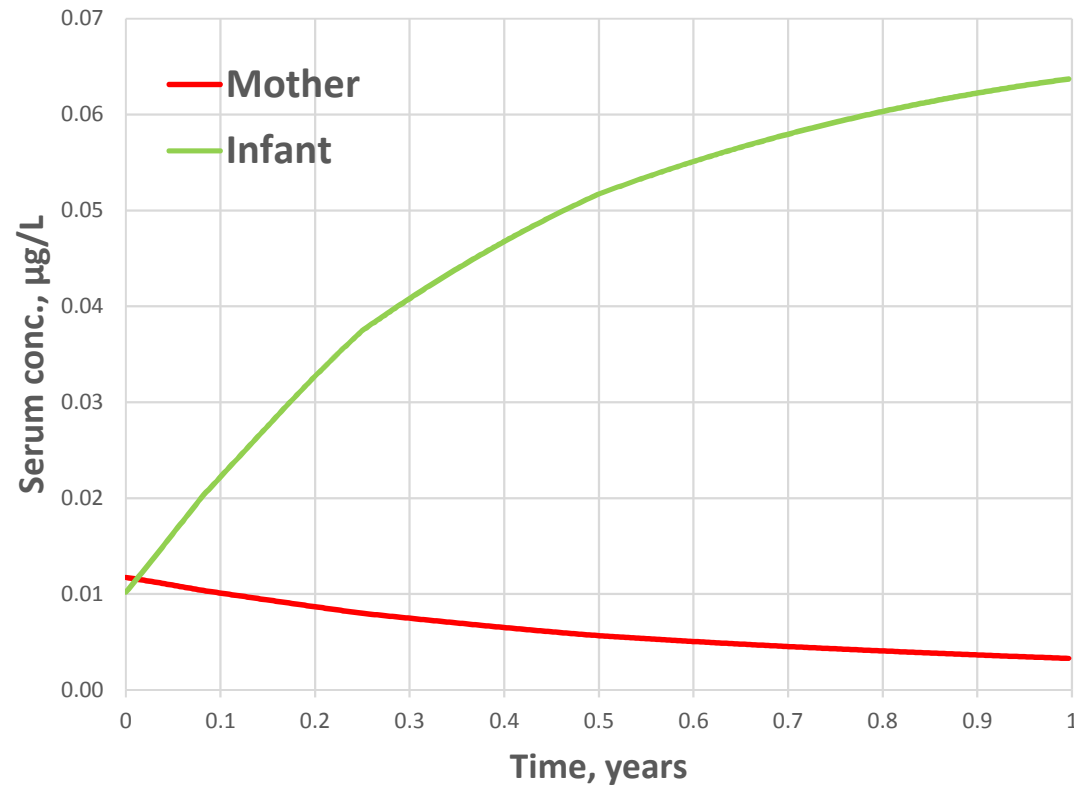
PFAS	Water conc., ug/L	Mother's serum, ug/L	Mother's milk, ug/L	Milk:Water ratio	Half-life, d
PFOA	0.035	11.7	0.61	17.4	delivery
		3.3	0.17	4.9	1 year
PFOS	(R)	(R)	(R)	6.2	1241
		(R)	(R)	4.4	
PFHxS	(R)	(R)	(R)	7.4	1935
		(R)	(R)	5.6	

(R) = redacted value pending public release

Why the big difference between breastfeeding and formula-feeding?
 PFAS concentration in milk can be much higher than the concentration in contaminated water

Breastfeeding vs. Formula feeding

Maternal and Infant PFOA Serum Concentrations
During 1 Year of Breastfeeding



Mother is effectively “offloading” body burden onto infant

Shape of curve will depend on chemical parameters

MDH still recommends breastfeeding to mothers due to myriad health benefits

Current and Future Steps

- ✓ PFOA guidance (0.035 ug/L) has been released
- ✓ Analysis of PFOS and PFHxS is complete
- ❑ Release of PFOS and PFHxS values and documentation next week
- ❑ Summer 2019 – anticipating release of NTP report on PFOA; will determine if revision of our PFOA value is warranted
- ❑ Also considering adapting model to evaluate fish consumption
- ❑ Monitoring continues around the state

For More Information

- See our recent open-access article in the *Journal of Exposure Science and Environmental Epidemiology*, 29:183-95, 2019.
<https://www.nature.com/articles/s41370-018-0110-5>
- Sign up for notifications about our upcoming guidance for PFOS and PFHxS: <https://bit.ly/2HTnRyQ>

Thanks!

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Key References

- Vd adjustment factors:

Friis-Hansen 1961. Body Water Compartments in Children: Changes During Growth and Related Changes in Body Composition. Pediatrics, 28(2)169-181.

- Model development:

MDH 2017. Background Document: Toxicokinetic Model for PFOS and PFOA and Its Use in the Derivation of Human Health-based Water Guidance Values. (available upon request).

- RSC factors:

US EPA 2000. US Environmental Protection Agency (EPA). Office of Water. Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health. EPA-822-B-00-004. October 2000.

- Water and breast milk intake rates:

US EPA 2011. Exposure Factors Handbook. <https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252>

Extra material

MDH Model in agreement
with human serum data

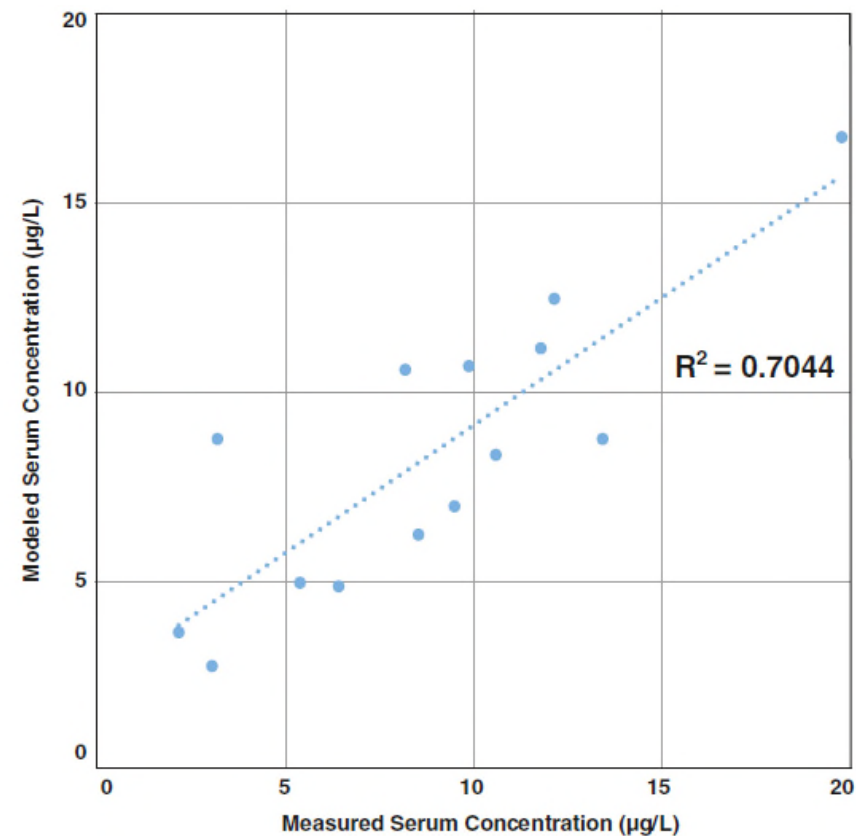
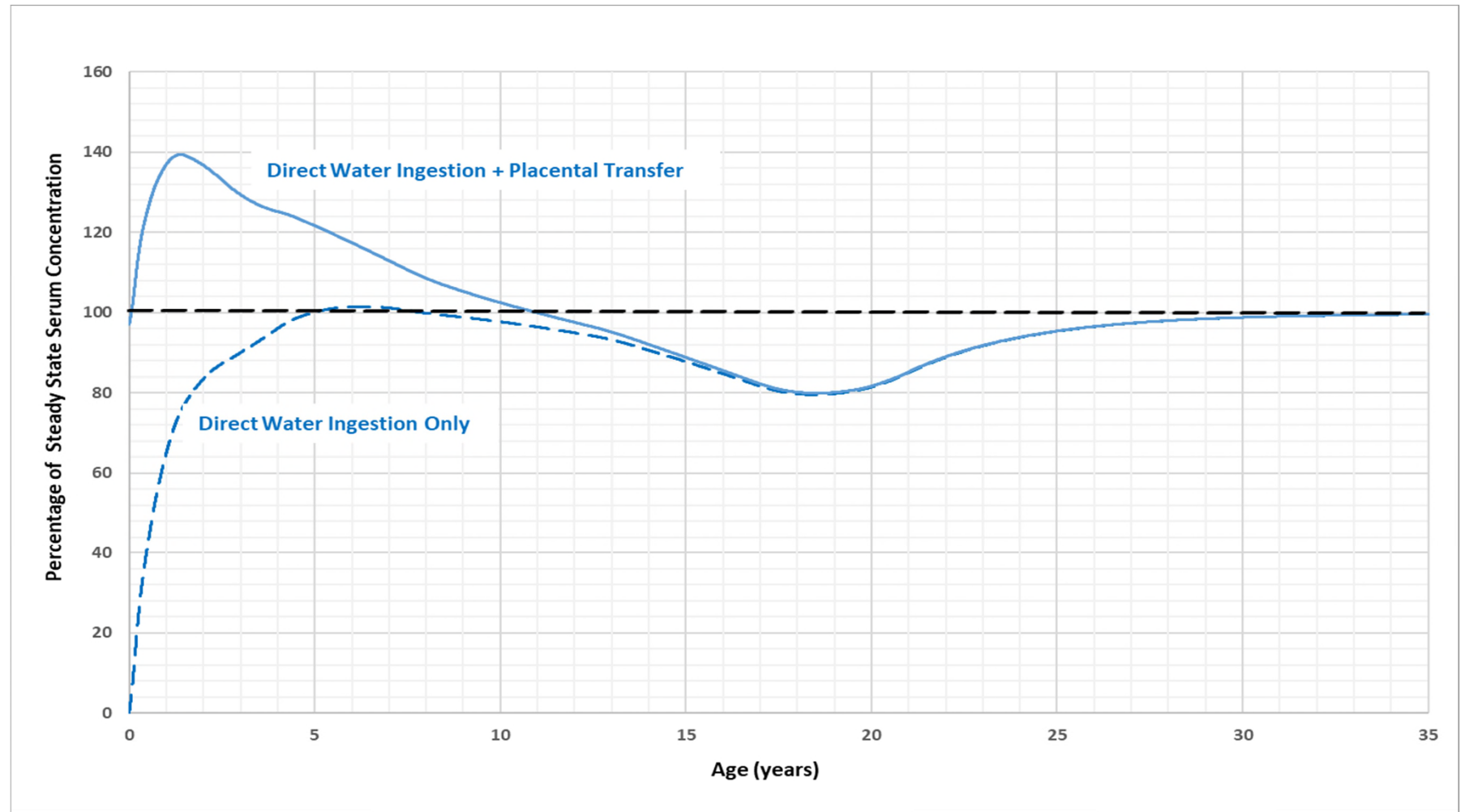


Fig. 5 Modeled individual infant PFOA serum concentration at 6 months of age versus measured levels estimated from Fromme et al. (Figure S6 [8])

Extra material

Placental Transfer has a large impact on serum levels



Extra material

Ingestion through breastmilk has an even larger impact

